REMARKS/ARGUMENTS

Claims 1-10, 13-22, and 36-38 are pending.

THE AMENDMENTS

The amendments to the specification (1) replace an originally-cited application number with the corresponding patent number for the patent that issued from the application; (2) identify cited trademarks more completely; and (3) correct two typographical errors. New claim 38 adds another dependent claim focusing on a particular form of the composition to be used in the claimed method.

None of the amendments presents new matter. The new claim is supported in the specification as filed, at page 9, lines 1-3. None of the amendments is intended in any manner to narrow the meaning or scope of any claim terms, for any reason of patentability or otherwise.

CORRECTION OF LISTED CLAIM FOR DOMESTIC PRIORITY

The Office Action acknowledges the claim for priority in the related PCT application and in the domestic provisional application under 35 U.S.C. § 119(e). However, Applicants also maintain their claim of priority in domestic utility application Ser. No. 09/668,384, filed 25 September 2000, in which the PCT application also claims priority. This claim of priority is correctly reflected in the declaration filed in this application. Accordingly, a request for corrected filing receipt has been submitted separately in this application, to correct the priority listing to add this domestic application.

THE REJECTIONS

Rejection of Claims For Nonstatutory Double Patenting

Claims 1-10, 36, and 37 are rejected under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claims 1-6 and 13-15 of U.S. Patent No. 6,126,959. The Examiner notes that while "the conflicting claims are not identical, they are not patentably distinct ... because the intended use limitations of the instant compositions do not patentably distinguish over '959 and the instant method claims would be inherent of the method claims in '959." The Examiner notes that a timely filed and compliant terminal disclaimer may be used to overcome this rejection.

Applicants respectfully disagree.

Claims 1-10, 36, and 37 of the instant application relate to compositions for treating endometriosis or infertility, or for improving fertility, using a ß-adrenergic agonist, such as terbutaline, with a bioadhesive cross-linked water-insoluble but water-swellable polycarboxylic acid polymer carrier, such as polycarbophil.

In contrast, claims 13 and 14 of the '959 patent relate to compositions and methods for vaginal delivery of a treating agent (other than progesterone or an anti-sexually transmitted disease agent) to achieve local efficacy without detrimental blood levels of the treating agent. Claim 15 relates to compositions for vaginal administration of a treating agent during menses. Thus, claims 13-15 relate to inventions that are very different from the subject matter of the instant claims, and thus cannot be deemed to make obvious the subject matter of the instant claims.

The mere disclosure of formulations and methods for targeted vaginal delivery of a treating agent while avoiding adverse blood levels cannot be deemed to make obvious the specific invention: use of particular treating agents to treat or improve specific conditions.

In particular, nothing in the '959 patent suggests or discloses that the instant compositions may be useful to treat endometriosis or infertility, or to improve fertility.

And claims 1-6 of the '959 patent relate to compositions that comprise a therapeutically effective amount of a ß-adrenergic agonist, such as terbutaline, with a bioadhesive cross-linked water-insoluble but water-swellable polycarboxylic acid polymer carrier, such as polycarbophil. Thus, these claims, too, relate to inventions very different from the subject matter of the instant claims. The conditions to be treated by the instant invention are different and distinct from any disclosed or discussed in the '959 patent. The instant claims relate to use of a ß-adrenergic agonist to treat endometriosis or infertility, or to improve fertility. As discussed further below, these conditions (and especially the improvement of fertility) are completely separate and distinct from the dysmenorrhea and premature labor discussed in the '959 patent, even though a certain proportion of women with endometriosis may experience dysmenorrhea as a symptom.

Applicants respectfully request that this rejection be reconsidered and withdrawn. Applicants reserve the right to enter a suitable terminal disclaimer at an appropriate time in order to vitiate this rejection, in the event that the rejection (1) is not overcome now or otherwise during prosecution, and (2) still applies to any claims that are allowed.

Rejection of Claims Under 35 U.S.C. § 102(e) - Harrison

Claims 1-3 and 6-10 are rejected as anticipated by Harrison U.S. Patent No. 6,197,327. Harrison is said to disclose a device and method for treating dysmenorrhea (primary or secondary), including the use of ß-adrenergic agonists such as terbutaline. "Examples of excipients include glycerin, mineral oil, polycarbophil, etc. (col. 2, lines 60-63)." Example 7, lines 5-10, is said to "teach the use of ibuprofen added to a gel comprising one of several different ingredients one of which is polycarbophil." The

Examiner also notes that the "drugs of the composition in example 9 can be substituted for the drugs in examples 4-7." Therefore, the Examiner concludes that "the use of terbutaline in the composition of example 7 containing polycarbophil is read on the claimed invention. Intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim."

Applicants respectfully disagree. Harrison relates to formulations specifically intended for treating dysmenorrhea. In stark contrast, the instant claims are directed to treating endometriosis or infertility, or to improving fertility. Endometriosis and, even more, fertility and infertility, are only peripherally associated with dysmenorrhea, at best.

Dysmenorrhea is defined typically as painful menstruation. Dysmenorrhea afflicts about 50% of menstruating women, with primary dysmenorrhea being much more common than secondary dysmenorrhea. See, for example, Taber's Cyclopedic Medical Dictionary (2001) ("Taber's") at pages 650-51 (copy attached). Primary dysmenorrhea usually begins just before or at menarche, and is thought to be associated with uterine ischemia and increased contractility due to increased production of prostaglandins. Id. at 650.

Secondary dysmenorrhea is described as potentially associated with many conditions, including not only endometriosis, but also pelvic inflammatory disease, use of an IUD, fertility problems related to imperforate hymen, uterine leiomyomas, adenomyosis, cervical stenosis, ovarian cysts, or pronounced uterine retroflexion and/or retroversion. Id. at 651. Treatment of secondary dysmenorrhea typically consists of administration of

nonsteroidal anti-inflammatory drugs for pain management, and can include medical or surgical management directed to relieve the underlying problem. Id.[1]

In contrast, endometriosis is a condition in which endometrial tissue has developed abnormally, extending outside the uterus. See, specification at page 1, lines 13-14; Taber's, at pages 702-03 (copy attached). Endometriosis is often accompanied by symptoms of dysmenorrhea with pelvic pain, premenstrual dyspareunia, sacral backache during menses, and infertility. Specification at page 1, lines 15-17; Taber's, at 702. Endometriosis is estimated to occur in 10% to 15% of actively menstruating women between the ages 25 and 44. Taber's at 702. Classic treatments of endometriosis typically attempt to mimic menopause or pregnancy, thereby also blocking ovulation. Specification at page 1, lines 21-27; Taber's, at 702. If necessary, surgery may be used to correct the condition. "The definitive treatment for endometriosis ends a woman's potential for pregnancy by removal of the uterus, tubes, and ovaries." Taber's, at 703.

Thus, there is no absolute or definite correlation between endometriosis and dysmenorrhea. Secondary dysmenorrhea may sometimes be (but is not always) a symptom of endometriosis, but there is no correlation at all between primary dysmenorrhea and endometriosis. Even secondary dysmenorrhea occurs frequently without concomitant endometriosis. And of course there is little or nothing in the record that suggests any correlation between dysmenorrhea and fertility or infertility.

Classical treatments for the different conditions are also very different. Treatment of secondary dysmenorrhea focus on providing relief of the pain and discomfort. Endometriosis frequently is treated with medical or surgical methods, such as tissue abatement or removal, or with hormone therapy directed to reduction of the abnormal tissue

[1] Note that primary dysmenorrhea may be treated with oral contraceptives or nonsteroidal anti-inflammatory drugs. See Taber's at page 651. However, as discussed above, this type of dysmenorrhea is not associated with endometriosis.

by maintaining a chronic state of anovulation. Thus, most treatments of dysmenorrhea would not be expected to treat endometriosis or infertility, or to improve fertility.

This is especially true with regard to the instant invention. The treating agents used, β-adrenergic agonists, are understood to inhibit muscle contractility, and thus are useful for treating or preventing dysmenorrhea or premature labor. Specification, at page 4, line 24 through page 5, line 8. But there is absolutely no teaching, recognition, or suggestion in Harrison or any other art of record that such treating agents could be used to treat endometriosis or infertility, or to improve fertility.

In fact, as set forth above, most prior art treatments of endometriosis tend to, temporarily if not permanently, preclude ovulation. According to Taber's, the "definitive treatment" for endometriosis ends a woman's potential for pregnancy. Taber's at 703. And hormonal therapies typically block ovulation, also preventing pregnancy at least temporarily. In stark contrast, the instant invention provides a treatment that itself acts to reduce infertility or improve fertility.

Applicants respectfully request that this rejection be reconsidered and withdrawn.

Rejection of Claims Under 35 U.S.C. § 102(e) - Harrison Evidenced By Peterson

Claims 13-19 and 22 are rejected as anticipated by Harrison as evidenced by Peterson U.S. Patent No. 6,207,696. Harrison is said to disclose a device and method for treatment of dysmenorrhea (primary or secondary), including the use of ß-adrenergic agonists such as terbutaline. As set forth above, the Examiner concluded that "the use of terbutaline in the composition of example 7 containing polycarbophil is read on the claimed invention." Peterson is relied on for teaching that "secondary dysmenorrhea **is** the pain associated with endometriosis (col. 4, lines 32-33)" (emphasis added). Therefore, the Examiner concluded that "a woman having dysmenorrhea resulting from endometriosis

would be given the composition of Harrison. The claiming of new use, new function, or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)."

Applicants respectfully disagree. Even the cited portion of Peterson, which in context appears to have been misread by the Examiner, belies the meaning suggested by the Examiner.

Peterson purports to provide a means for delivering a treating agent to the uterus, for relief of "prostaglandin-mediated disorders of the female reproductive system, by using histidine as the therapeutically active agent." Col. 4, lines 25-29. Peterson notes that prostaglandins "are at work, for example, in primary dysmenorrhea (frequently given the short-hand abbreviation "menstrual cramping"), secondary dysmenorrhea, **in** the pain associated with endometriosis, in pre-term or premature labor, and in other instances of uterine hypercontractility and ischemia." Col. 4, lines 30-35 (emphasis added). Thus, the cited portion of Peterson is not suggesting that dysmenorrhea "is" the pain associated with endometriosis, as suggested in the Office Action. Rather, Peterson merely lists both dysmenorrhea and the **pain** associated with endometriosis -- **not** endometriosis itself -- as two separate, distinct conditions associated with prostaglandins.

Thus clarified, the disclosure of Peterson, even together with Harrison, does not establish a direct connection between dysmenorrhea and the pain associated with endometriosis, let alone with endometriosis itself. Thus, these references combined do not render obvious the instant claims even with regard to endometriosis, let alone infertility or fertility. Applicants respectfully request that this rejection be reconsidered and withdrawn.

Rejection of Claims Under 35 U.S.C. § 102(e) - Peterson

Claims 6 and 7 are rejected as anticipated by Peterson. Peterson is said to teach "compositions and methods for the treatment of dysmenorrhea, endometriosis. Peterson teaches histidine as a therapeutically active agent (col. 4, lines 26-44). However, column 8, lines 48 through column 9, line 5 teaches that another therapeutically active agent ... useful for treating endometrial pain such as ß-adrenergic agonists i.e. terbutaline."

Applicants respectfully disagree. Peterson's disclosure, in context, is not consistent with the characterization and description.

First, as mentioned above, Peterson addresses use of histidine for treatment for certain prostaglandin mediated disorders, including dysmenorrhea and **the pain** associated with endometriosis -- not for treating the endometriosis itself.

Second, Peterson discusses situation wherein it may be advantageous to co-administer histidine with "one or more additional therapeutically active agents" preferably at a lower than normal dose. Column 8, lines 48-58. Such secondary agents include separately "agents which are useful for abating or treating disorders such as dysmenorrhea and pre-term labor, agents for treating endometrial pain (e.g., NSAIDs, hormones), and agents for treating underlying reproductive disorders which as a result of correction or abatement cause dysmenorrhea." Column 8, line 63 to Column 9, line 2.

Peterson separately lists "Examples of therapeutic agents for treating dysmenorrhea" and "Representative therapeutic agents for treating endometriosis," at Column 9, lines 3-26, and lines 26-32. Most importantly, **ß-adrenergic agonists are included only in the list of agents for treating dysmenorrhea, and not in the list for treating endometriosis.** Id. Thus, Peterson does not suggest that ß-adrenergic agonists such as terbutaline may be useful in treating endometriosis.

Peterson cannot reasonably be said to teach or disclose the use of ß-adrenergic agonists to treat endometriosis. If anything, Peterson's listing of ß-adrenergic agonists for treating dysmenorrhea, and the absence of those same agents from Peterson's list of treating agents for endometriosis, could instead be seen as teaching away from the use of ß-adrenergic agonists to treat endometriosis.

Applicants respectfully request that this rejection be reconsidered and withdrawn.

Rejection of Claims Under 35 U.S.C. § 103(a) - Harrison In View Of Peterson

Claims 4, 5, 20, 21, 36, and 37 are rejected as obvious over Harrison in view of Peterson, as described above. "As for the limitation of % weight and dosage regimen it would be routinely determined by one of ordinary skill in the art, through minimal experimentation."

Applicants respectfully disagree. As discussed above, Harrison addresses only the treatment of dysmenorrhea. And Peterson does not disclose or teach that dysmenorrhea "is the pain associated with endometriosis," or that endometrial pain -- let alone endometriosis itself -- may be treated with ß-adrenergic agonists. And there simply is no disclosure, teaching, or suggestion that fertility may be improved, or that infertility may be treated, with ß-adrenergic agonists.

Thus, even the combination of Harrison and Peterson do not render obvious the instant invention with regard to endometriosis, infertility, or fertility. Applicants request that this rejection be reconsidered and withdrawn.

Conclusion

In light of these remarks, Applicants respectfully request reconsideration and withdrawal of all rejections, and allowance of all claims.

No fee is believed to be due for this submission. If any fees are due, please charge the required fees to Winston & Strawn Deposit Account No. 501-814.

Respectfully submitted,

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